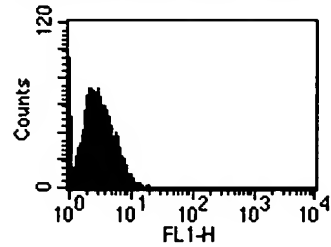


FIGURE 1

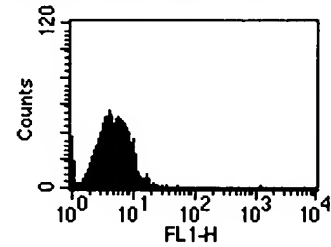
Y1251F IGF-I Receptor Cells

Insulin Receptor Cells

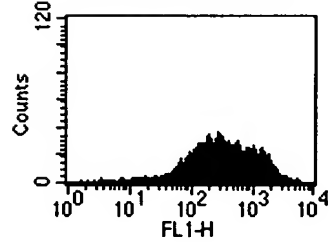
Goat α mouse-IgG-FITC only



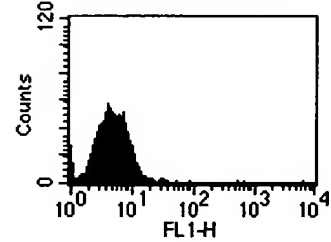
Goat α mouse-IgG-FITC only



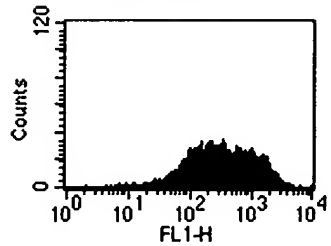
100 nM α EM164



100 nM α EM164



100 nM α 1H7



100 nM α IR

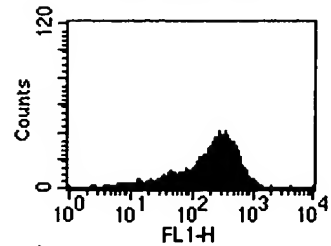


FIGURE 2

**Titration curve for binding
of EM164 antibody to
biotinylated IGF-I Receptor**

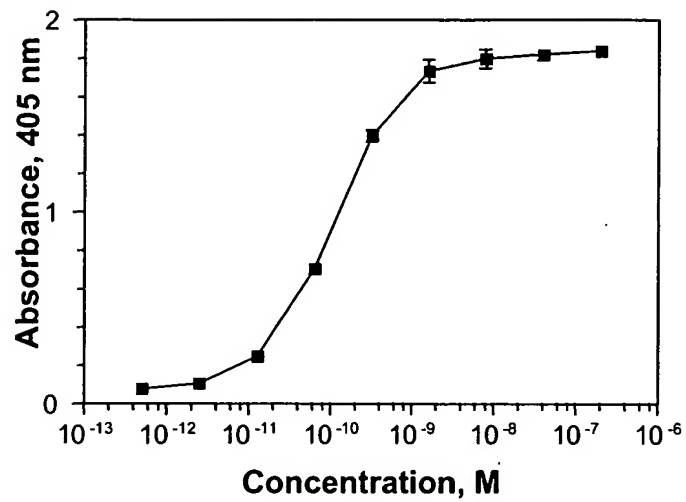


FIGURE 3

**Inhibition of binding of biotin-IGF-I
to MCF-7 Cells by EM164 antibody**

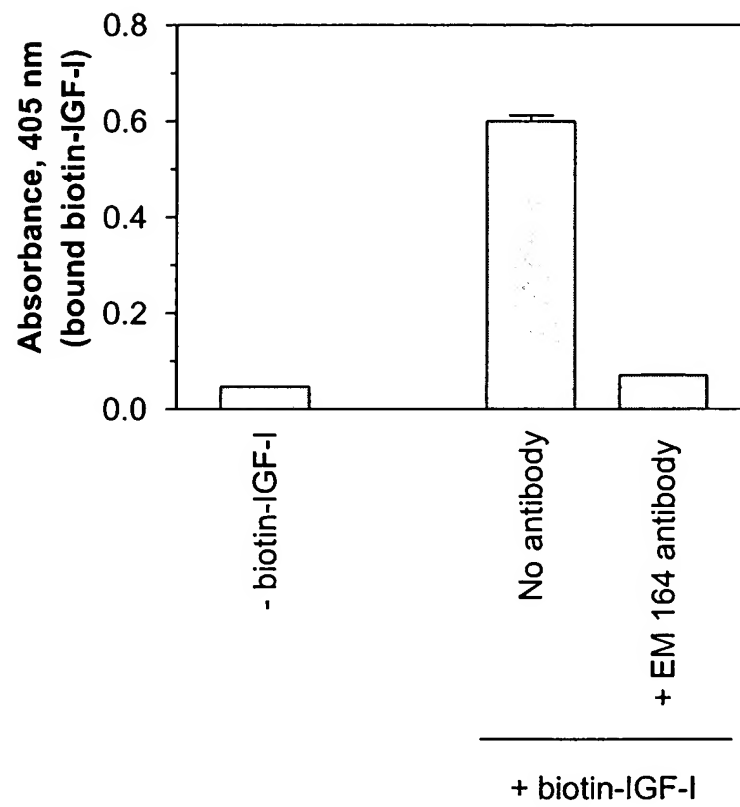


FIGURE 4

Inhibition of IGF-I-Stimulated Autophosphorylation of IGF-I Receptor in MCF-7 Cells by EM164 Antibody

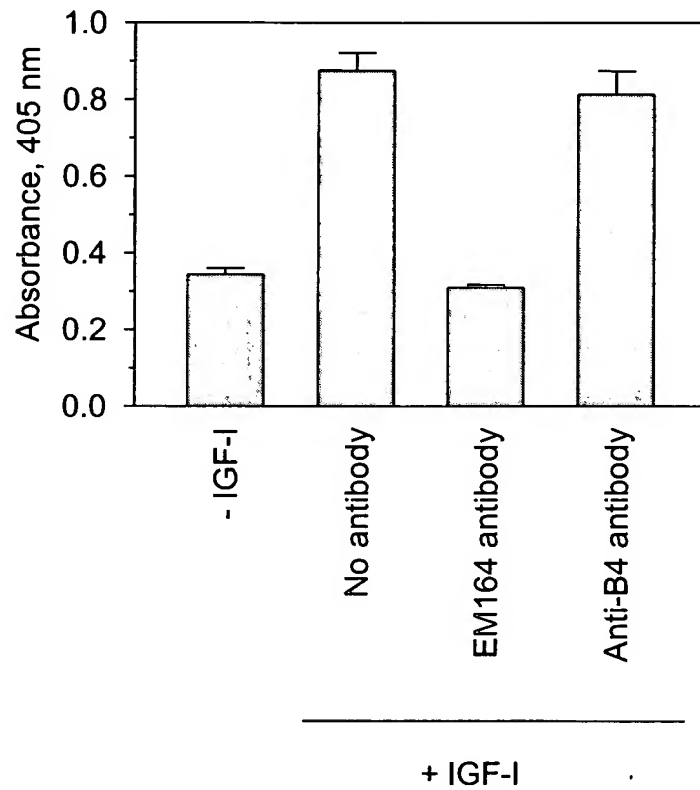


FIGURE 5

**Inhibition of IGF-I-Stimulated IRS-1-Phosphorylation
in MCF-7 Cells by EM 164 antibody**

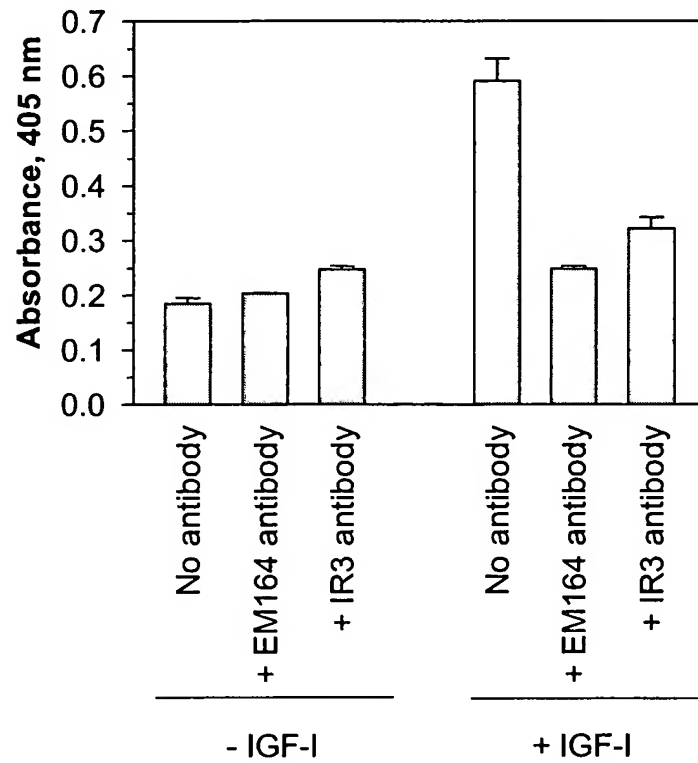


FIGURE 6

**Inhibition of IGF-I-Stimulated Signal Transduction
 in SaOS-2 Cells by EM164 Antibody**

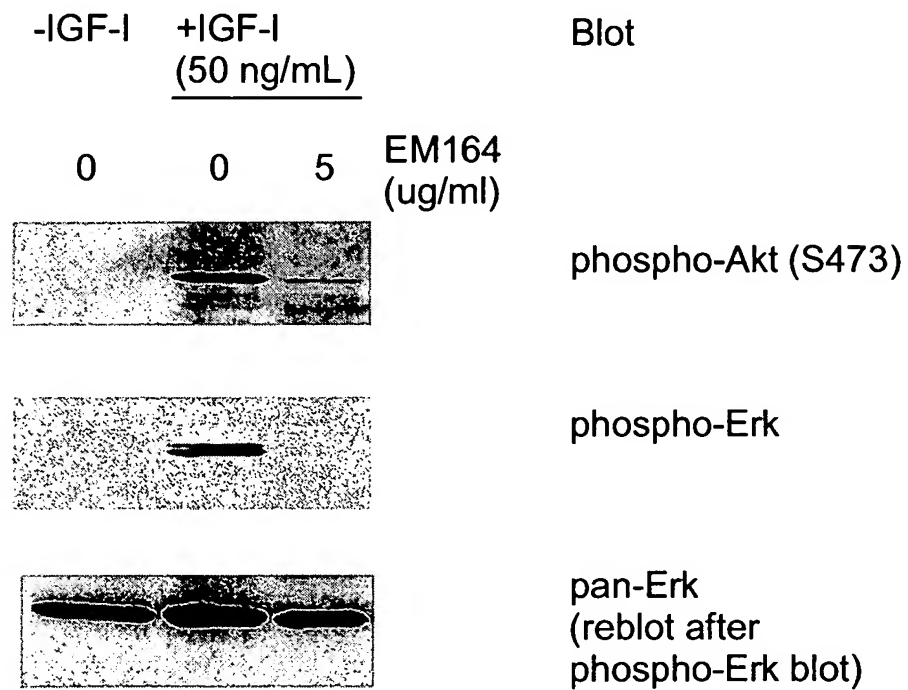


FIGURE 7

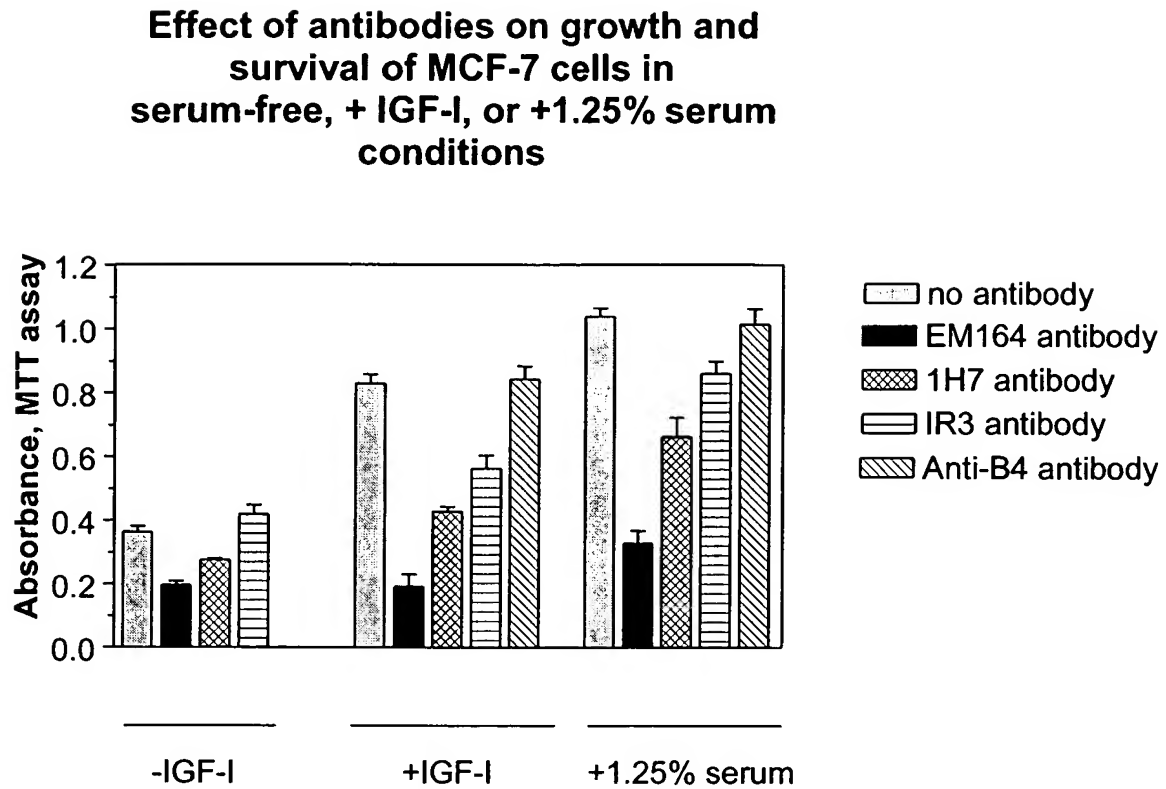


FIGURE 8

Effect of EM164 antibody on growth and survival of MCF-7 cells in 0.04 - 10% serum

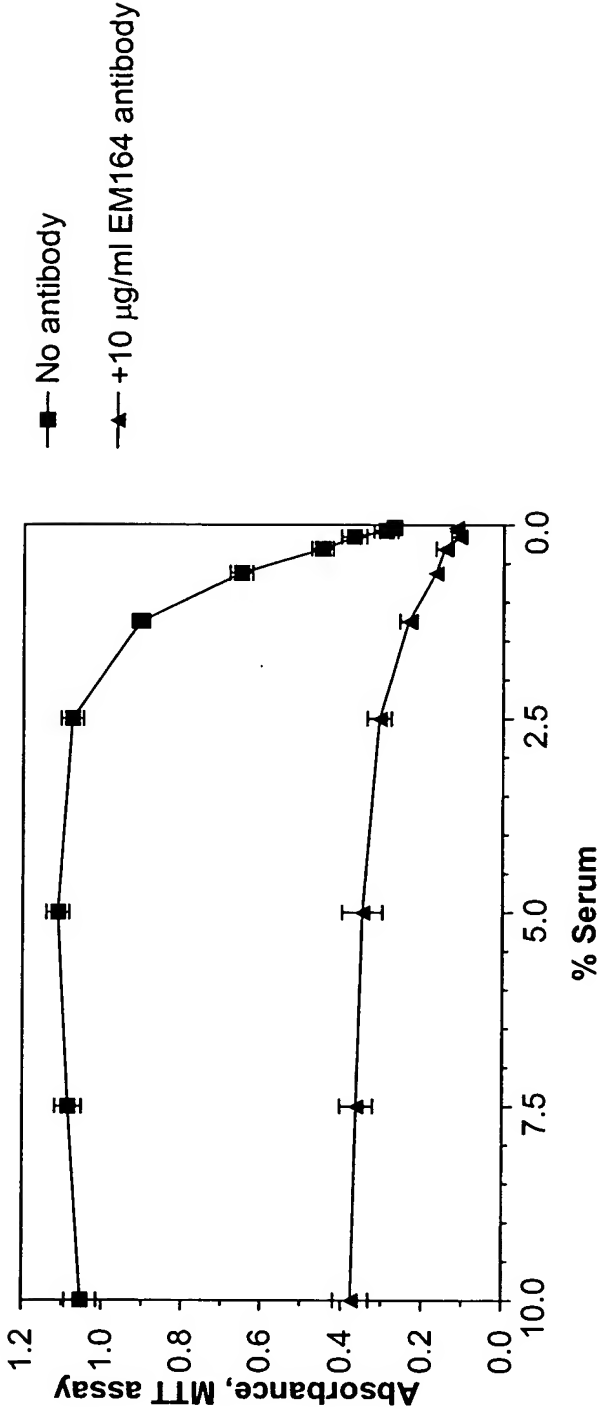


FIGURE 9

**Inhibition of IGF-I- and
 serum-stimulated growth and
 survival of NCI-H838 cells**

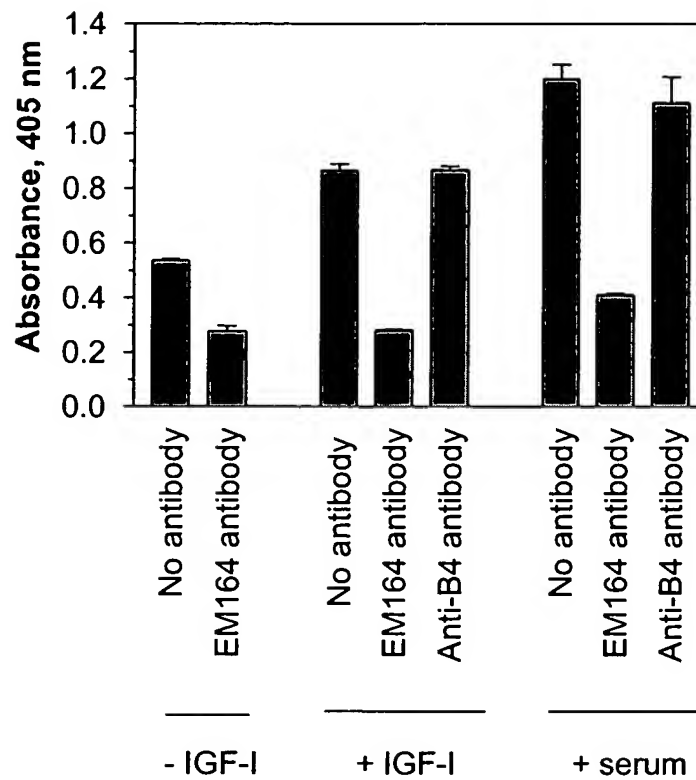


FIGURE 10

Effect of treatment with EM164 antibody, or taxol, or a combination of EM164 antibody and taxol, on growth of Calu-6 lung cancer xenograft in mice

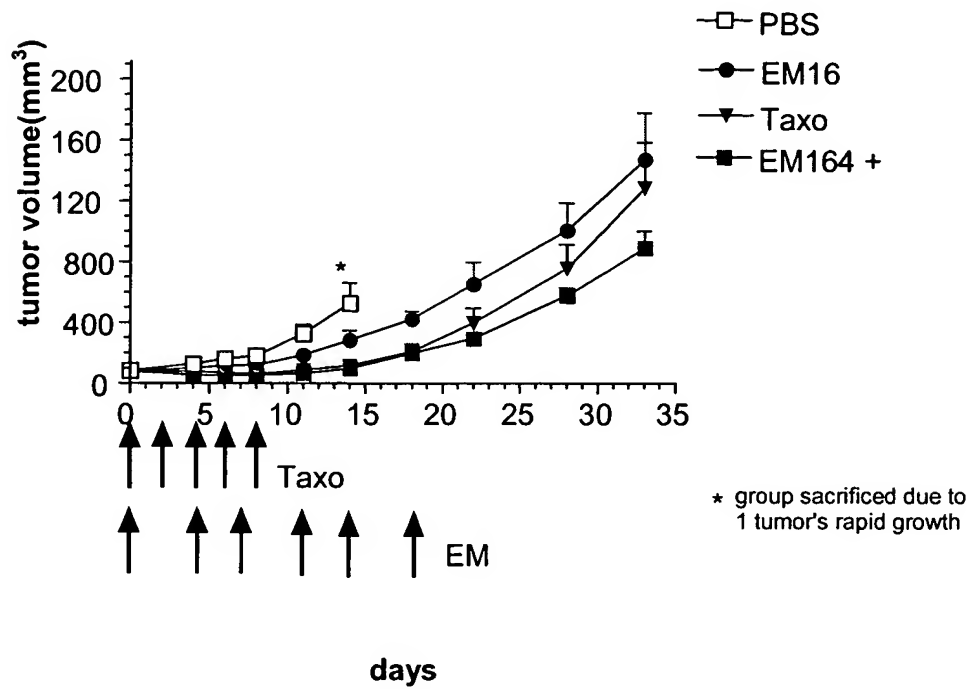


FIGURE 11

Competition of binding of humanized EM164 antibody (version 1.0) to immobilized biotinylated IGF-I receptor by murine EM164 antibody (1.06 to 10.6-fold molar concentration range)

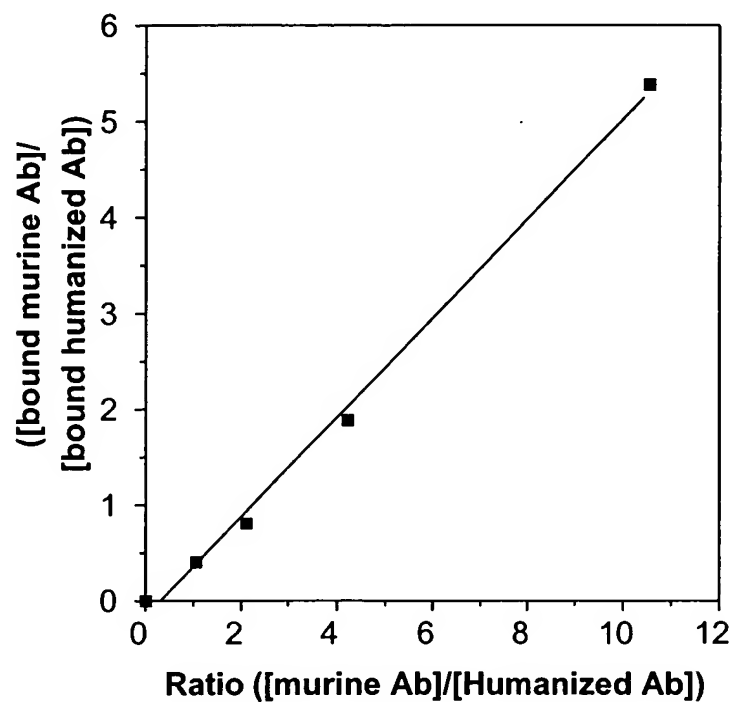


FIGURE 12

→
Murine EM164 Light Chain

```

1 atgaagttgcctggttaggctggttggtgctgatgttctggattcct
1  M K L P V R L L V L M F W I P

46 gcttccagtagtgatggtttgatgacccaaactccactctccctg
16  A S S S D V L M T Q T P L S L
    -VK

91 cctgtcagtccttgagatcaagcctccatctcttgagatctagt
31  P V S L G D Q A S I S C R S S
                               CDR1

136 cagagcattgtacatagtaatgtaaacacctatttagaatggtac
46  Q S I V H S N V N T Y L E W Y
      CDR1

181 ctgcagaaaccaggccagtcctcaaagctcctgatctacaaagtt
61  L Q K P G Q S P K L L I Y K V
                               CDR2

226 tccaaccgattttctgggggtcccagacaggttcagtggcagtgga
76  S N R F S G V P D R F S G S G
      CDR2

271 tcagggacagatttcacactcaggatcagcagagtggaggctgag
91  S G T D F T L R I S R V E A E

316 gatctgggaattttattactgctttcaagggttcacatgttcctccg
106 D L G I Y Y C F Q G S H V P P
                               CDR3

361 acgttcggtggaggcaccaagctggaaatcaaacgg
121 T F G G G T K L E I K R
  
```

FIGURE 13

→
Murine EM164 Heavy Chain

```

1 atgggatggagctatatcatcctctttttggtagcaacagctaca
1  M G W S Y I I L F L V A T A T

46 gaagtccactcccaggtccaactgcagcagtcctggggctgaactg
16  E V H S Q V Q L Q Q S G A E L
    -VH

91 gtgaagcctggggcttcagtgaagctgtcctgtaaggcttctggc
31  V K P G A S V K L S C K A S G

136 tacaccttcaccagctactggatgcactgggtgaagcagaggcct
46  Y T F T S Y W M H W V K Q R P
           CDR1

181 ggacaaggccttgagtggattggagagattaatcctagcaacggt
61  G Q G L E W I G E I N P S N G
                        CDR2

226 cgtactaactacaatgagaagttcaagaggaaggccacactgact
76  R T N Y N E K F K R K A T L T
           CDR2

271 gtagacaaatcctccagcacagcctacatgcaactcagcagcctg
91  V D K S S S T A Y M Q L S S L

316 acatctgaggactctgcggtctattactttgcaagaggaagacca
106 T S E D S A V Y Y F A R G R P
                                CDR3

361 gattactacggtagtagcaagtggtaacttcgatgtctggggcgca
121 D Y Y G S S K W Y F D V W G A
           CDR3

406 gggaccacgggtcacctgtctcctca
136 G T T V T V S S

```

FIGURE 14

Murine EM164 CDRs

Light Chain

CDR1: R S S Q S I V H S N V N T Y L E

CDR2: K V S N R F S

CDR3: F Q G S H V P P T

Heavy Chain

CDR1: S Y W M H

CDR2: E I N P S N G R T N Y N E K F K R

CDR3: G R P D Y Y G S S K W Y F D V

AbM Heavy Chain

CDR1: G Y T F T S Y W M H

CDR2: E I N P S N G R T N

CDR3: G R P D Y Y G S S K W Y F D V

FIGURE 15

Germline sequence comparisons

Light Chain		50
Cr1	- DVLMTQTPLSLPVSLGDQASISCRSSQSIVHSNGNTYLEWYLQKPGQSPK	
muEM164	- -----V-----	
Cr1	- LLIYKVSNRFSGVDPDRFSGSGSGTDFTLKISRVEAEDLGVYYCFQGSHVP	100
muEM164	- -----R-----I-----	
Heavy Chain		50
J558.c	- QVQLQQPGAELVKPGASVKLSCKASGYTFTSYWMHWVKQRPGQGLEWIGE	
muEM164	- -----S-----	
J558.c	- INPSNGRTNYNEKFKSKATLTVDKSSSTAYMQLSSPTSEDSAVYYCAR	98
muEM164	- -----R-----L-----F--	

FIGURE 16

Cloning and Mammalian Expression Plasmid Maps

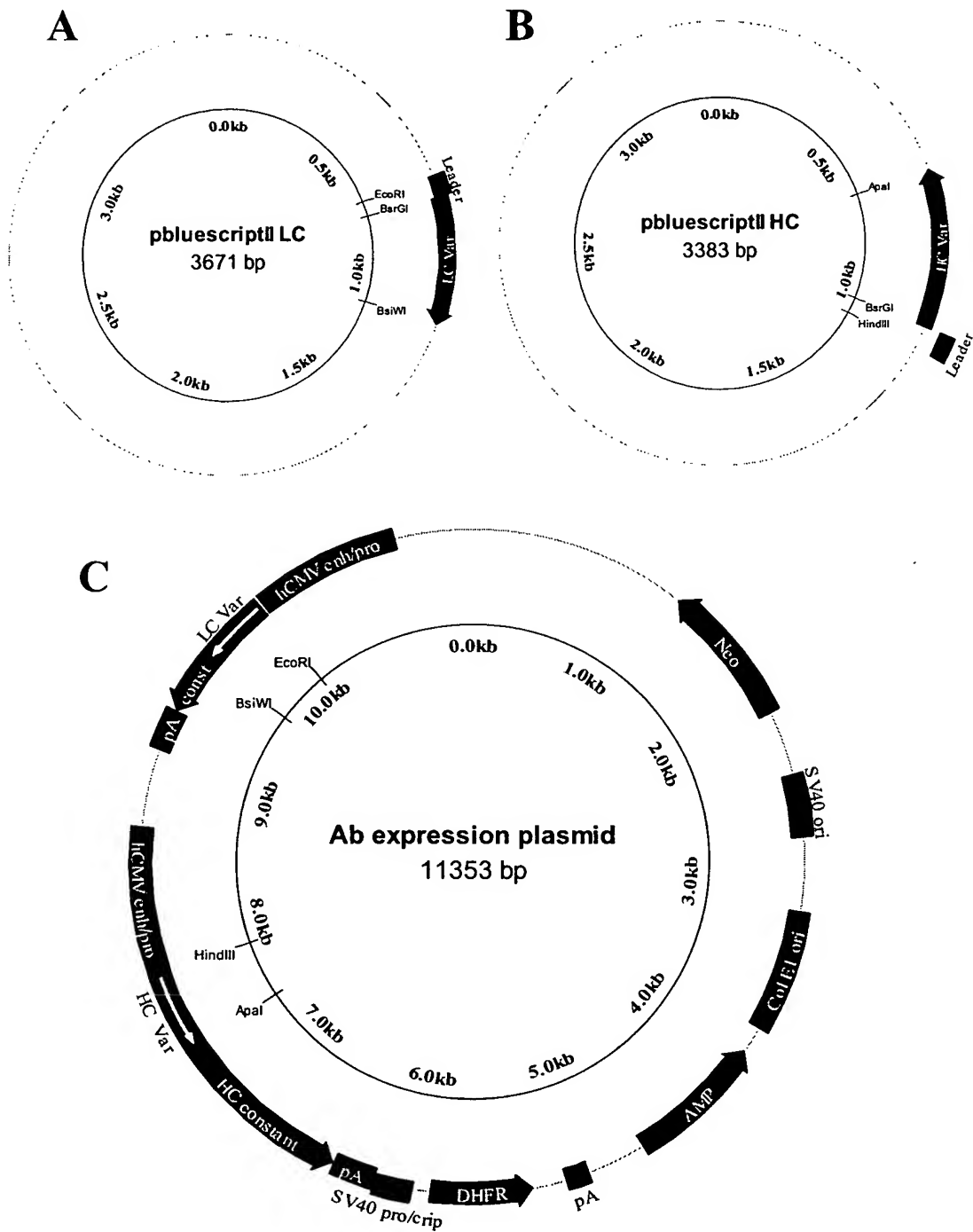


FIGURE 17

10 Most Homologous Light Chain Sequence Alignment

	1	10	20	30	40	50
em164 LC	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPK
2jel	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGNTYLEW	YLQKPGQSPK
2pcp	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGNTYLEW	YLQKPGQSPK
lnqb	DIEL	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGNTYLEW	YLQKPGQSPK
lkel	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGNTYLEW	YLQKPGQSPK
lhyx	ELVM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGDITYLEW	FLQKPGQSPK
ligf	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	LSDGDTYLEW	YLQKPGQSPK
ltet	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSSGNTYLEW	YLQKPGQSPK
lclz	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HNNGNTYLEW	YLQKPGQSPK
lbln	DVLM	TQTPLS	LSVSLGDQAS	ISCRSSQSIV	HSTGNTYLEW	YLQKPGQSPK
lcly	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HNNGNTYLEW	YLQKPGQSPK
Consensus	d v l m T Q t P l S	L p V S L G D Q A S	I S C R s s Q x i v	h s n g n t Y l e W	y L Q K p G Q S P k	

	60	70	80	90	100
em164 LC	LLIYKVS	NRFSGVPDRFSGS	GS GTDFTLKI	SRVEAEDLG	IVYYCFQGSHVP
2jel	LLIYKVS	NRFSGVPDRFSGS	GS GTDFTLKI	SPVQAEDLG	VYYCFQGSSEVP
2pcp	LLIYKVS	NRFSGVPDRFSGS	GS GTDFTLKI	SRVEAEDLG	VYYCFQGSSEVP
lnqb	LLIYKVS	NRFSGVPDRFSGS	GS GTDFTLKI	SRVEAEDLG	VYYCFQGSSEVP
lkel	LLIYKVS	NRFSGVPDRFSGS	GS GTDFTLKI	SRVEAEDLG	VYYCFQGSSEVP
lhyx	LLIYKVS	NRFSGVPDRFSGS	GS GTDFTLKI	SRVEAEDLG	VYYCFQGSSEVP
ligf	LLIYKVS	NRFSGVPDRFSGS	GS GTDFTLKI	SRVEAEDLG	VYYCFQGSSEVP
ltet	LLIYKVS	NRFSGVPDRFSGS	GS GTDFTLKI	SRVEAEDLG	VYYCFQGSSEVP
lclz	LLIYKVS	NRFSGVPDRFSGS	GS GTDFTLKI	SRVEAEDLG	VYYCFQGSSEVP
lbln	LLIYKVS	NRFSGVPDRFSGS	GS GTDFTLKI	SRVEAEDLG	VYYCFQGSSEVP
lcly	LLIYKVS	NRFSGVPDRFSGS	GS GTDFTLKI	SPVEAEDLG	VYYCFQGSSEVP
Consensus	L L I Y k v s n r f	S G V P D R F S G S	G S G T D F T L k i	S R V e A E D L G v	Y Y C F Q g s H v P

	110	120	130	140	150
em164 LC	PTFGG	GTKLE	IKR		
2jel	YTFGG	GTKLE	IKR		
2pcp	YTFGG	GTKLE	IKR		
lnqb	YTFGG	GTKLE	IKR		
lkel	RTFGG	GTKLE	IKR		
lhyx	PTFGG	GTKLE	IKR		
ligf	PTFGG	GTKLE	IKR		
ltet	FTFGS	GTKLE	IKR		
lclz	FTFGS	GTKLE	IKR		
lbln	RTFGG	GTKLE	IKR		
lcly	FTFGS	GTKLE	IKR		
Consensus	x T F G g G T K L E	I K R			

FIGURE 18

10 Most Homologous Heavy Chain Sequence Alignment

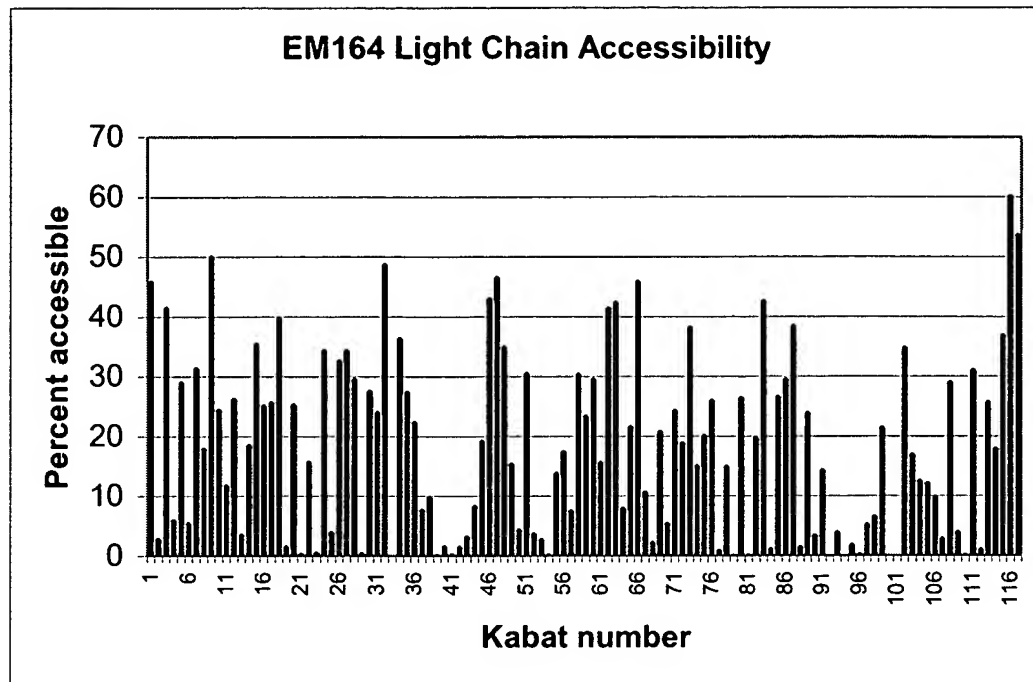
	1	10	20	30	40	50
em164 HC	QVQLQQSGAE	LVKFGASVFL	SCRASGYTFT	SYWMHNVFQR	PGQGLEWIGE	
lnqb	QVQLQQSGAE	LVKFGASVFL	SCRASGYTFT	SYWMHNVFQR	PCRGLWIGR	
lngp	QVQLQQPGAE	LVKFGASVFL	SCRASGYTFT	SYWMHNVFQR	PCRGLWIGR	
lfbi	QVQLQQPGAE	LVKFGASVFL	SCRASGYTFT	SYWMHNVKQG	PGQGLEWIGE	
lafv	QVQLQQPGSV	LVRFJASVFL	SCRASGYTFT	SSWIHNAKQR	PGQGLEWIGE	
lyuh	QVQLQQSGAE	LVKFGASVFL	SCRASGYTFT	SYLMHNVFQR	PCRGLWIGR	
lp1g	QIQQLQQSGPE	LVRFGASVFI	SCRASGYTFT	DYYIHNVKQR	EGEGLEWIGW	
ld5b	QVQLQQSGAE	LMKFGASVFI	SCRATGYTFS	SFWIEEVKQR	PGHGLEWIGE	
lae6	QIQQLQQSGPE	LVKFGASVFI	SCRASGYTFT	DYYINNMELK	PGQGLEWIGW	
laxs	QVQLLESAGAE	LMKFGASVFI	SCRATGYTFS	SFWIEEVKQR	PGHGLEWIGE	
3hfl	-VQLQQSGAE	LMKFGASVFI	SCRASGYTFS	DYWIEEVKQR	PGHGLEWIGE	
Consensus	q v Q l q q s G a e	L v k P G A S V K x	S C K A s G Y T F t	s y w x h W v K Q r	P G x G L E W I G x	

	60	70	80	90	100
em164 HC	INPNSNGRTNY	NEKFKRKATL	TVDKSSSTAY	MQLSSLTSED	SAVYYFARGR
lnqb	IDPNSGGTKY	NEKFKSKATL	TVDKPSSTAY	MQLSSLTSED	SAVYYCAR--
lngp	IDPNSGGTKY	NEKFKSKATL	TVDKPSSTAY	MQLSSLTSED	SAVYYCAR--
lfbi	IDPNSGYPNY	NEKFKGKATL	TVDKSSSTAY	MQLSSLTSED	SAVYYCAS--
lafv	IHPNSGNTNY	NEKFKGKATL	TVDTSSTAY	VDLSSLTSED	SAVYYCAR--
lyuh	IDPNNVVTKF	NEKFKSKATL	TVDKPSSTAY	MQLSSLTSED	SAVYYCAR--
lp1g	IYFGSGGNTKY	NEKFKGKATL	TVDTSSTAY	MQLSSLTSED	SAVYYCAR--
ld5b	ILEGSGGTHY	NEKFKGKATF	TADKSSNTAY	MQLSSLTSED	SAVYYCARGH
lae6	IDPFGSGNTKY	NEKFKGKATL	TVDTSSTAY	MQLSSLTSED	SAVYYCAR--
laxs	ILEGSGGTHY	NEKFKGKATF	TADKSSNTAY	MQLSSLTSED	SAVYYCARGH
3hfl	ILEGSGSTNY	HERFKGKATF	TADTSSTAY	MQLNSSLTSED	SGVYYCLHGN
Consensus	I x P x s g x t x y	n E k F K g K A T l	T v D k s s s T A Y	m q L s s L T S E D	s a v Y y c a r - -

	110	120	130	140	150
em164 HC	PDYVGSSKWKY	FQVWGAGTTV	TVSS		
lnqb	YDYVGSS--Y	FQVWGAGTTV	TVSS		
lngp	YDYVGSS--Y	FQVWGAGTTL	TVSS		
lfbi	LYYVGTSYGV	LDYWGAGTSV	TVSS		
lafv	-WRVYGSP--Y	FQVWGAGTTL	TVSS		
lyuh	YAYCRP----	MDYWGAGTTV	TVSS		
lp1g	--GK--FA	MDYWGAGTSV	TVSS		
ld5b	S--YF--YD	GQYWGAGTSV	TVSS		
lae6	--EKTYYA	MDYWGAGTSV	TVSA		
laxs	S--YF--YD	GQYWGAGTSV	TVSS		
3hfl	-----YD	FQVWGAGTTL	TVSS		
Consensus	x x y y x x x - x x	x D y W G q G T x v	T V S S		

FIGURE 19

A.



B.

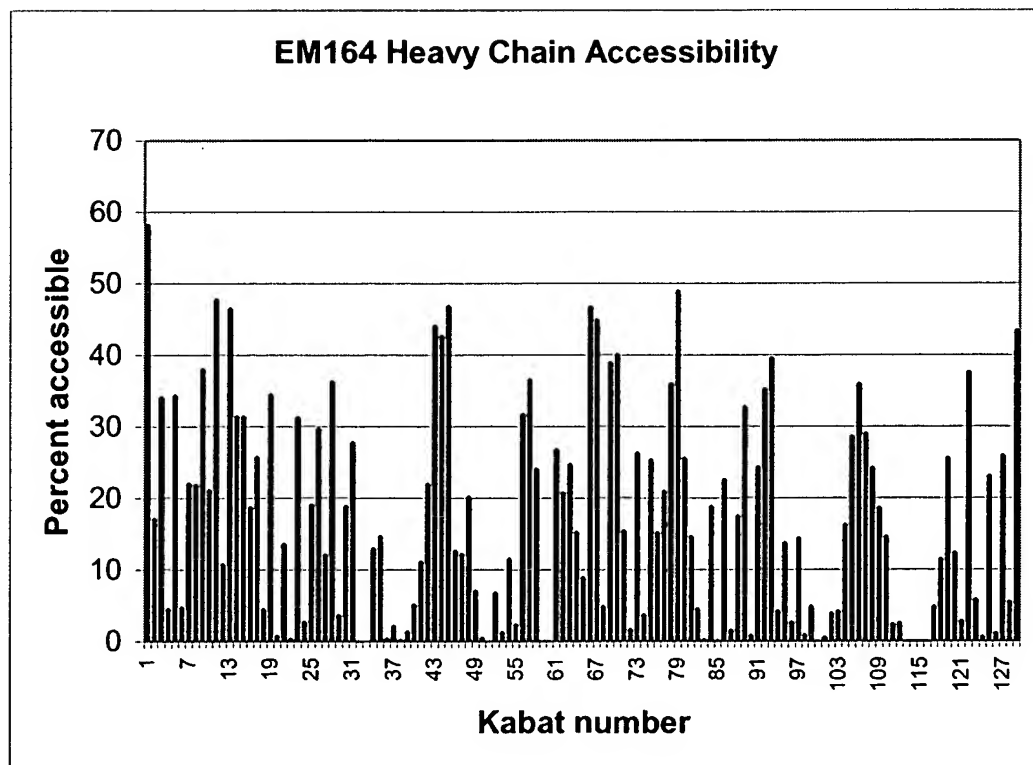


FIGURE 20

**Light Chain Variable Region Amino Acid Sequences for
Murine and Humanized EM164 Antibodies**

Kabat #	1	10	20	27c	35	45
muEM164	DVLMTQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPK	
huEM164 v1.0	DVVMQTPLS	LPVSLGDPAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPR	
huEM164 v1.1	DVLMTQTPLS	LPVSLGDPAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPK	
huEM164 v1.2	DVLMTQTPLS	LPVSLGDPAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPR	
huEM164 v1.3	DVVMQTPLS	LPVSLGDPAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPK	
changes	*		*			*

Kabat #	46	55	65	75	85	95f
muEM164	LLIYKVSNR	SGVPDRFSGS	GSGTDFTLRI	SRVEAEDLGI	YYCFQGSHVP	
huEM164 v1.0	LLIYKVSNR	SGVPDRFSGS	GAGTDFTLRI	SRVEAEDLGI	YYCFQGSHVP	
huEM164 v1.1	LLIYKVSNR	SGVPDRFSGS	GAGTDFTLRI	SRVEAEDLGI	YYCFQGSHVP	
huEM164 v1.2	LLIYKVSNR	SGVPDRFSGS	GAGTDFTLRI	SRVEAEDLGI	YYCFQGSHVP	
huEM164 v1.3	LLIYKVSNR	SGVPDRFSGS	GAGTDFTLRI	SRVEAEDLGI	YYCFQGSHVP	
changes			*			

Kabat #	96	105	108
muEM164	PTFGGGTKLE	IKR	
huEM164 v1.0	PTFGGGTKLE	IKR	
huEM164 v1.1	PTFGGGTKLE	IKR	
huEM164 v1.2	PTFGGGTKLE	IKR	
huEM164 v1.3	PTFGGGTKLE	IKR	
changes			

FIGURE 21

**Heavy Chain Variable Region Amino Acid Sequences for
 Murine and Humanized EM164 Antibodies**

Kabat #	1	10	20	30	40	50
muEM164	QVQLQQSGAE	LVKPGASVKL	SCKASGYTFT	SYWMHWVKQR	PGQGLEWIGE	
huEM164	QVQLVQSGAE	VVKPGASVKL	SCKASGYTFT	SYWMHWVKQR	PGQGLEWIGE	
changes	*	*				
Kabat #	51	59	69	79	86	96
muEM164	INPSNGRTNY	NEKFKRKATL	TVDKSSSTAY	MLSSLTSED	SAVYYFARGR	
huEM164	INPSNGRTNY	NQKFQGKATL	TVDKSSSTAY	MLSSLTSED	SAVYYFARGR	
changes		*	**			
Kabat #	97	100f	109	113		
muEM164	PDYYGSSKWY	FDVWGAGTTV	TVSS			
huEM164	PDYYGSSKWY	FDVWGQGTTV	TVSS			
changes		*				

FIGURE 22

huEM164 v1.0 Variable Region DNA and Amino Acid Sequences
Light Chain

```

1 gatgttgtgatgacccaaactccactctccctgcctgtcagtctt
1 D V V M T Q T P L S L P V S L

46 ggagatccagcctccatctcttgcagatctagtcagagcatagta
16 G D P A S I S C R S S Q S I V

91 catagtaatgtaaacacctatttagaatggtacctgcagaaacca
31 H S N V N T Y L E W Y L Q K P

136 ggccagtctccaaggctcctgatctacaaagtttccaaccgattt
46 G Q S P R L L I Y K V S N R F

181 tctggggtcccagacaggttcagtggcagtggagcagggacagat
61 S G V P D R F S G S G A G T D

226 ttcacactcaggatcagcagagtggaggctgaggatctgggaatt
76 F T L R I S R V E A E D L G I

271 tattactgctttcaaggttcacatgttcctccgacgttcggtgga
91 Y Y C F Q G S H V P P T F G G

316 ggcaccaaactggaaatcaaacgt
106 G T K L E I K R

```

Heavy Chain

```

1 caggtccaactggtgcagtctggggctgaagtgggaagcctggg
1 Q V Q L V Q S G A E V V K P G

46 gcttcagtgaagctgtcctgtaaggcttctggctacaccttcacc
16 A S V K L S C K A S G Y T F T

91 agctactggatgcactgggtgaagcagaggcctggacaaggcctt
31 S Y W M H W V K Q R P G Q G L

136 gagtggattggagagattaatcctagcaacggtcgtactaactac
46 E W I G E I N P S N G R T N Y

181 aatcagaagttccagggaaggccacactgactgtagacaaatcc
61 N Q K F Q G K A T L T V D K S

226 tccagcacagcctacatgcaactcagcagcctgacatctgaggac
76 S S T A Y M Q L S S L T S E D

271 tctgcggtctattactttgcaagaggaagaccagattactacggt
91 S A V Y Y F A R G R P D Y Y G

316 agtagcaagtggctacttcgatgtctggggccaagggaaccaggtc
106 S S K W Y F D V W G Q G T T V

361 accgtctcctca
121 T V S S

```

FIGURE 23

**huEM164 v1.1, 1.2, 1.3 Light Chain Variable Region DNA
and Amino Acid Sequences**

v1.1

```

1 gatgttttgatgacccaaactccactctccctgcctgtcagtctt
1 D V L M T Q T P L S L P V S L

46 ggagatccagcctccatctcttgcagatctagtcagagcatagta
16 G D P A S I S C R S S Q S I V

91 catagtaatgtaaacacctatttagaatggtacctgcagaaacca
31 H S N V N T Y L E W Y L Q K P

136 ggccagtctccaaagctcctgatctacaaagtttccaaccgattt
46 G Q S P K L L I Y K V S N R F

181 tctgggggtcccagacaggttcagtggtcagtgaggcagggacagat
61 S G V P D R F S G S G A G T D

226 ttcacactcaggatcagcagagtgagggtgaggatctgggaatt
76 F T L R I S R V E A E D L G I

271 tattactgctttcaaggttcacatgttcctccgacgttcggtgga
91 Y Y C F Q G S H V P P T F G G

316 ggcaccaaactggaaatcaaacgt
106 G T K L E I K R

```

v1.2

```

1 gatgttttgatgacccaaactccactctccctgcctgtcagtctt
1 D V L M T Q T P L S L P V S L

46 ggagatccagcctccatctcttgcagatctagtcagagcatagta
16 G D P A S I S C R S S Q S I V

91 catagtaatgtaaacacctatttagaatggtacctgcagaaacca
31 H S N V N T Y L E W Y L Q K P

136 ggccagtctccaaaggtcctgatctacaaagtttccaaccgattt
46 G Q S P R L L I Y K V S N R F

181 tctgggggtcccagacaggttcagtggtcagtgaggcagggacagat
61 S G V P D R F S G S G A G T D

226 ttcacactcaggatcagcagagtgagggtgaggatctgggaatt
76 F T L R I S R V E A E D L G I

271 tattactgctttcaaggttcacatgttcctccgacgttcggtgga
91 Y Y C F Q G S H V P P T F G G

316 ggcaccaaactggaaatcaaacgt
106 G T K L E I K R

```

(FIGURE 23, CONT.)

v1.3

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1 gatgttgtgatgacccaaactccactctccctgcctgtcagtcctt
1 D V V M T Q T P L S L P V S L

46 ggagatccagcctccatctcttgcagatctagtcagagcatagta
16 G D P A S I S C R S S Q S I V

91 catagtaatgtaaacacctatTTtagaatggtacctgcagaaacca
31 H S N V N T Y L E W Y L Q K P

136 ggccagtctccaaagctcctgatctacaaagtttccaaccgattt
46 G Q S P K L L I Y K V S N R F

181 tctgggggtcccagacagggttcagtggtcagtgaggcagggacagat
61 S G V P D R F S G S G A G T D

226 ttcacactcaggatcagcagagtgagggtgaggatctgggaatt
76 F T L R I S R V E A E D L G I

271 tattactgctttcaagggttcacatgttctccgacgttcggtgga
91 Y Y C F Q G S H V P P T F G G

316 ggcaccaaactggaaatcaaacgt
106 G T K L E I K R
```


FIGURE 24
Comparison of inhibition of IGF-I-stimulated growth and survival of MCF-7 cells by humanized EM164 v1.0 antibody (6-25 μ g/mL) vs murine EM164 antibody (5-10 μ g/mL)

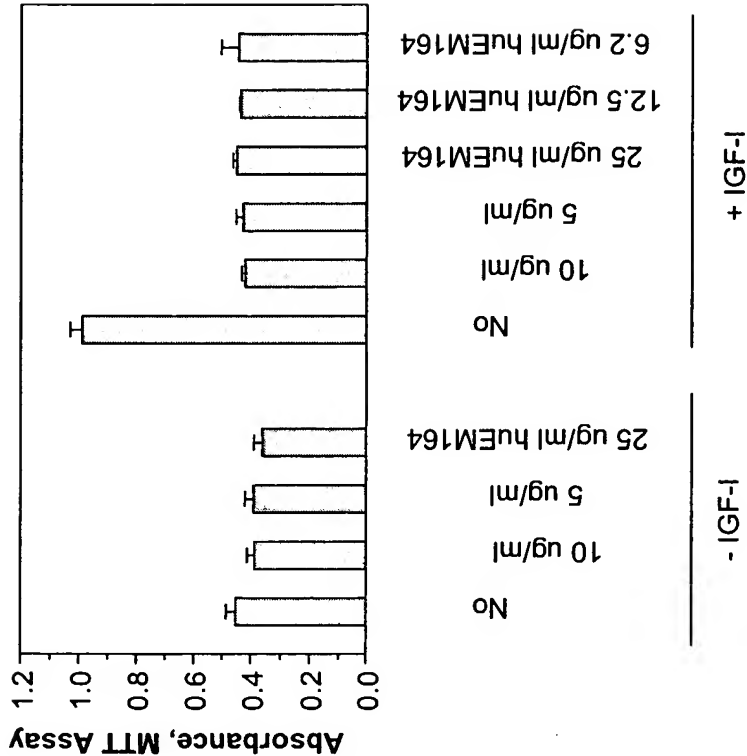


FIGURE 25

Cell cycle arrest of MCF-7 cells by EM164 antibody

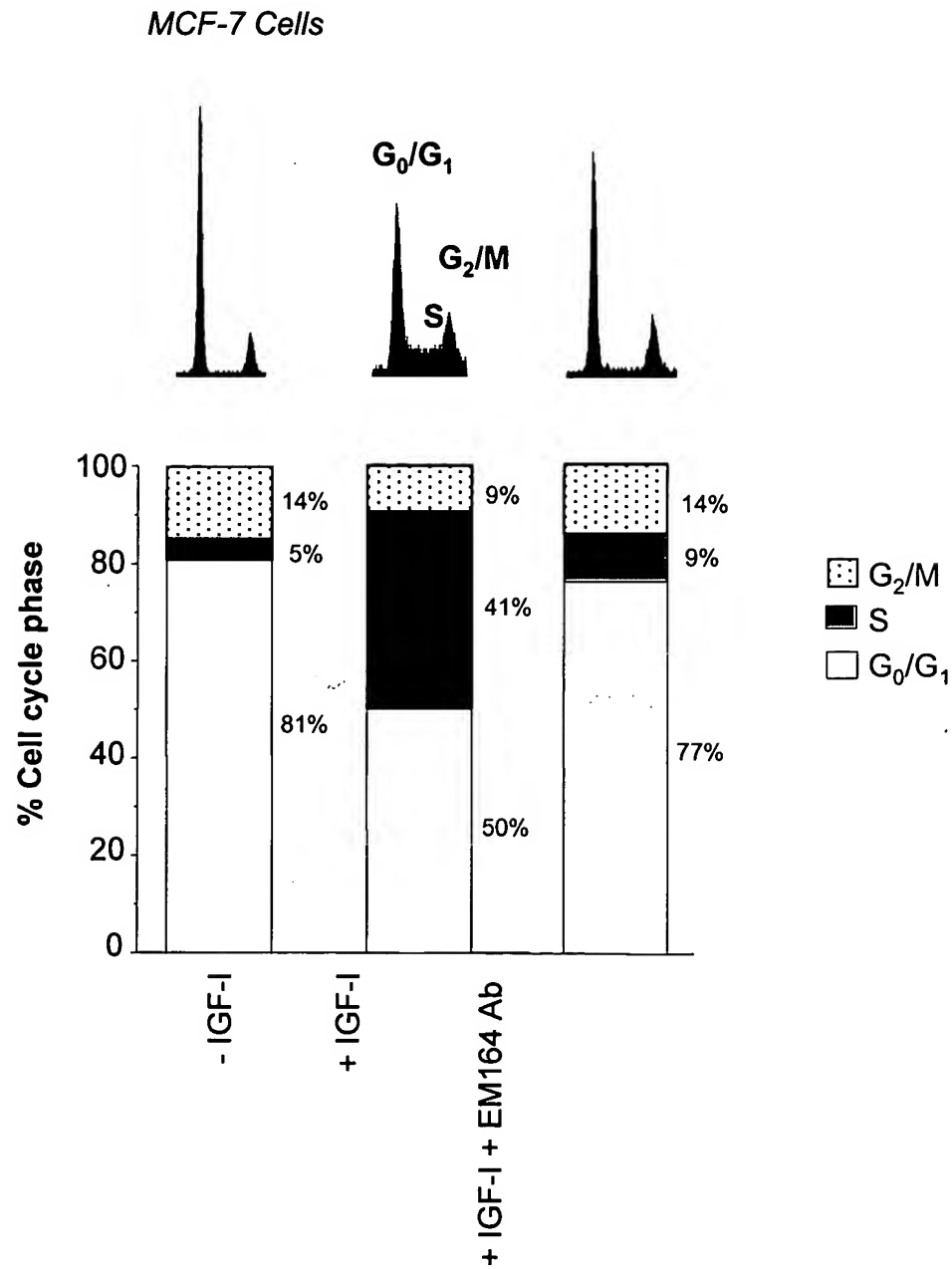


FIGURE 26

**Induction of apoptosis in NCI-H838 lung cancer cells by EM164 antibody
(measured from the cleavage of cytokeratin CK18 protein by caspase)**

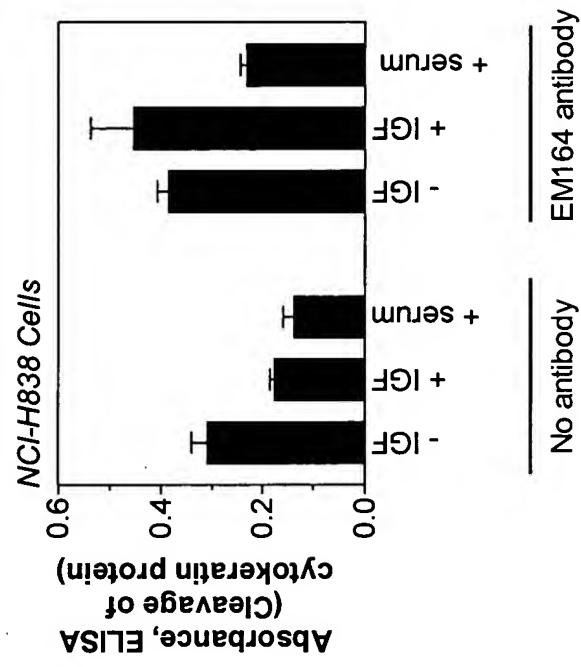


FIGURE 27

Suppression of growth of BxPC-3 human pancreatic cancer xenografts in mice by EM164 antibody treatment as a single agent or in combination with gemcitabine

